Diagnostic and Prognostic role of CA125 with patients of ovarian cancer .

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Abstract

To evaluate the diagnostic and prognostic significant of CA125 test , within a fallow up of three months , and its role for monitoring response to treatment by chemotherapy . To evaluate serum C-reactive protein (CRP) as a prognostic variable in patients with ovarian cancer . This study was conducted in Mosul . Iraq from January 2007 through July 2009 . A sample of 44 consecutive women aged from (35-55 years) and suffering from ovarian cancer with control group of 45 women were included in this study . A pre-tested questionnaire was employed to obtain information on family history to this disease , laporatomy treatment if present , asking for benign disease of the uterus , liver and gastro intestinal tract and benign tumors of ovaries & uterus if present specially for control group . Physical examination by C.T. scans and ultra sounds were then done . Blood samples were collected for 89 women and measurement of CA125 and CRP were performed . Serum from 44 patients participant were analyzed for CA125 and CRP before and after treatment with chemotherapy and laporatomy if present at three months interval for fallow up mean ± SD for these patients before chemotherapy course was 78.42 ± 14.6 U/ml for CA125 in which CRP concentration for 37 patients of this group at the same period of time was 96 mg/dl 84.1% (group 1) and the remainder 7 patients was 48 mg/dl 15.9 % (group 2) . There was a significant differences for CA125 value in patients before therapy and according to period of therapy at $P<0.01$. CRP concentration was 96 mg/dl still high after one month of chemotherapy , its value was decrease in the second and third month of chemotherapy . Preoperative determination of CA125 may play a good role the prognosis of post operative chemotherapy . It may be useful to included this test in the diagnosis of ovarian cancer with the help of physical examination in future .

Introduction

The ovarian cancer mucine CA125 was first identified by the monoclonal antibody OC125 in 1981, but its genetic structure has been determined only recently [(1)] .
CA125 a mucin like glycoprotein of molecular weight > 200000 KDa [(2)] , but lower glycoprotein recognized by a monoclonal antibody which was raised using an ovarian cancer cell line as immunogen[(3)].The CA125 molecule is composed of a short cytoplasmic tail a trans membrane domain ,and an exceptionally larg glycosylated extra cellular domain dominated by in excess of 66-156 amino acid repeat unites known to bind the antibodies OC125and M11.This large

glycosylated mucine molecule is present with in normal ovarian tissue and on the epithelium of endometerium , and fallopian tubes , however its precise cellular function is yet known[1,2].

CA125 is an one fetal antigen used as tumor marker in various malignancies, especially in those originating from the female reproductive tract or gastrointestinal organs [4] .

CA125 is currently the only tumor marker to have a well defined and validated role in the monitoring of ovarian cancer [5], decreasing levels are associated with response to therapy increasing levels with tumor progression [5,6,7,8]. Despite this correlation , most patients with a normal CA125 (< 30 units / ml) and no clinical evidence of disease at the completion of primary chemotherapy still microscopic residual cancer [5] .

CA125 has also been shown to be an accurate marker to define progression of ovarian cancer , and because elevated on an average (3 to 4 months before clinically assessable symptomatic, palpable , or visible by imagining) disease in 70% of patients [9] .

A pre-tested questionnaire was employed to obtained information on family history to this disease laporatomy treatment if present , benign disease of the uterus , liver , gastro intestinal and benign tumors of the ovarian and uterus if present specially for control group . Physical examination by C.T. scan & ultra sound of the ovaries which was then done .

A cancer antigen 125 (CA 125) is protein found on the surface of many ovarian cancer cell , it also can be found in other cancers and in small amounts in normal tissue . CA125 test measures the amount of this protein in the blood , it is well established as an accurate reliable means of monitoring response to treatment and confirming relapse in ovarian cancer patients . we therefore determined what change accurate predictor of relapse in patients on follow up after therapy for ovarian cancer with the aid of CRP which play a good role in the prognosis of this disease .

Statistical analysis data were analyzed using the statistical pack ages for social sciences (SPSS) . Unpainted Z-test was used to assess the significance of difference between mean values . Duncan's test was used to identify group(s) responsible for statistical difference in comparison . All values are quoted as the mean ± SD . Differences between objectives were considered significant at $P<0.05$ [10] .

Aim of the present study was to evaluate the diagnostic and prognostic significant of CA125 , within a follow up of 3 months , and its role for monitoring response to treatment by chemotherapy , and to evaluate serum C-reactive protein (CRP) as a prognostic variable in patients with ovarian cancer.

Patients & Methods

Forty-four consecutive women aged from (35-55 years) and suffering from ovarian cancer having a CA125 (96%) from the patients before underwent a chemotherapy was double of the CA125 from a baseline value (with a minimum baseline at the upper limit of normal, usually 30 U/ml were included in this study . During the study period from January 2007 through July 2009 in Mosul Province in Northern Iraq , the general clinical practice for

surveillance of ovarian cancer patients achieving a complete clinical and radiographic response at oncology and nuclear medicine hospital and Ibn Sina teaching hospital . which was using important to complete physical examination. CA 125 and CRP levels were measured every month for 3 months interval to follow up the patient before each course of chemotherapy in which, CRP was measured before this treatment too. CA125 was measured in archived sera stored at -20 ◦c while CRP measured immediately .

Forty-five patients were included in this study as a control group. In which CA125 in 20 women (44.4%) was ≥30 U/ml, while the reminder 25 (55.6%) was < 30 U/ml .
Serum CA125 II were measured by the use of minividas, which was an automated test for use on the VIDAS instruments, for the measurement of OC125 antigenic determinants in human serum or plasma using ELFA technique (Enzyme Linked Fluorescent Assay) [(11)] using a kit purchased from biomereux Ltd, France CRP was measured using fresh sera by CRP latex test [(12)], using a kit purchased from plasmatic Ltd, London .

Results

Serum from 44 patients participant were analyzed for CA125 and CRP before and after treatment with chemotherapy and laboratory if present at three months interval for follow up mean ± SD for these patients before chemotherapy course was 78.42 ± 14.6 U/ml for CA125 in which CRP concentration for 37 patients of this group at the same period of time was 96 mg/dl (84.1%) (group 1) and the remainder 7 patients was 48 mg /dl (15.9%) (group 2) .
First month of chemotherapy meant ± SD was (49.14±10.9 U/ml) p<0.001 for CA125 , CRP for group 1 was 34 patients 77.3% , for group 2 was 10 patients 22.7% .
Second month of chemotherapy meant ± SD was (27.97±12.7 U/ml) P<0.001 for CA125 , CRP concentration for group 1 was 14 patients 31.8% for group 2 was 30 patients 68.2% p<0.001 .
Third month after chemotherapy mean ± SD was (20.25±8.8 U/ml) p< 0.001 for CA 125 ,CRP concentration was 4 patients (9.1%) p<0.001 for both group of patients . see table 1&2 , fig 1& 2.
All the patients having a value of CA125 > 30 U/ml before hemotherapy laporatomy if present , after one month of chemotherapy the value still >30 U/ml while in the second month 17 patients 38.6% was > 30 U/ml and the remainder 27 patients 61.4% having a value < 30 U/ml while in the third month of chemotherapy this value still > 30 U/ml just in 5 patients 11.4 % and 39 patients 88.6% lesser than 30 U/ml . see table 3-fig3 Distribution of CRP concentration in patients before and during chemotherapy has been shown in fig 4, in which before chemotherapy There was a significant differences between CA125 value (58.08±22.58 U/ml) and CRR concentration in group 1 of patients p<0.05 , also between CA125 value (38.09 ± 21.45 U/ml) and CRP concentration was 96 mg/dl still high after one month of chemotherapy , it's value was decrease in the second and third month of chemotherapy.
CRP concentration in group 2 of patients p<0.05 , while in those patients having a CRP concentration of 6 and 12 mg/dl , there was no significant differences with CA125 value p>0.05 . see table 4 .

Sensitivity and specificity of CA125 as a diagnostic indicator has been shown in table 5, in which , sensitivity of CA125 was 100%

Discussion

CA125 is an antigenic determinant of a high molecular weight glycoprotein recognized by the murine monoclonal antibody OC-125 as performed by a routine blood test . It has an established role in monitoring treatment and detecting recurrence of ovarian cancer and has been advocated as a prognostic marker for advanced ovarian cancer [13,14,15,16,17] .

The CA125 antigen is not specific for ovarian cancer , as serum increase were observed in some patients with cancers of the breast , endometrium , gastro intestinal tract , and lung . Benign disease of the uterus, liver , and gastro intestinal tract and benign tumors of the ovaries & uterus are also associated with increased concentrations of serum CA125 [3, 18,19] while its specificity was 55.6% $p<0.001$ and for CRP was 100% for the first one and 33.3% for the second $p<0.001$.

Although CA125 test is not recommended as a screening test for ovarian cancer at this time , CA 125 test with ultrasound and C.T. scan as a second line test may be used to test women who have a high chance for ovarian cancer [8,20] , therefore determined what change in CA 125 level was the most accurate predictor of relapse in patients on follow up after therapy for ovarian cancer beside CRP, which was used to evaluate the prognostic variable in patients with ovarian cancer [21] , as it shown in the result .

The lack of specificity CA125 for ovarian cancer has not hampered the use of the test in the clinical management of patients with this disease . Initially , the CA 125 test was approved for use postoperatively in patients to determine the like hood of that tumor would be found at a second look operation . [19,3,2] .

In which patients whose CA125 levels fall to within the normal range after chemotherapy , a doubling of CA125 from the upper limit has been shown to predict tumor progression accurately [22,23] , which is seen in one case of this study .

Although this study does not include preoperative determination of CA 125 (just 2 cases with a level twice time more than the upper limit) but the data support the hypothesis that the prognosis of patients with postoperative serum CA-125 $\leq$ 30 U/ml is extremely good if they receive a full surgical staging [13] . Therefore , the preoperative serum CA125 value should be included to the decision making for postoperative chemotherapy .

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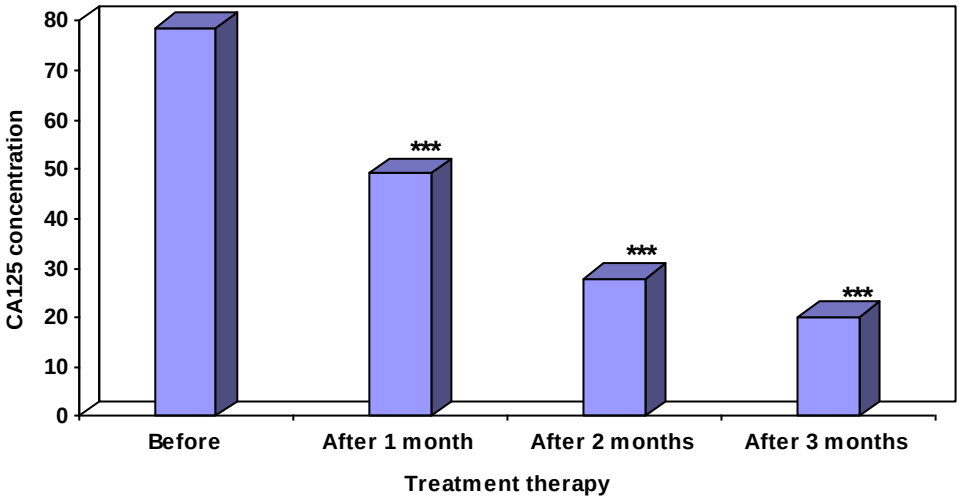
Table 1 : Comparison of CA125 concentration in patients before and after therapy at different periods.

Therapy period (month)	Mean ± SD		p-value
	Before therapy	After therapy	
1	78.42 ± 14.6	49.14 ± 10.9	<0.001
2	78.42 ± 14.6	27.97 ± 12.7	<0.001
3	78.42 ± 14.6	20.25 ± 8.8	<0.001

Using paired t-test

Table 2 : Distribution of CRP concentration in patients before and during therapy.

CRP	Before therapy		After 1 month		After 2 months		After 3 months	
	No.	%	No.	%	No.	%	No.	%
<6	0	0.0	0	0.0	0	0.0	19	43.2
12	0	0.0	0	0.0	0	0.0	16	36.4
18	0	0.0	0	0.0	0	0.0	1	2.3
48	7	15.9	10	22.7	30	68.2	4	9.1
96	37	84.1	34	77.3	14	31.8	4	9.1

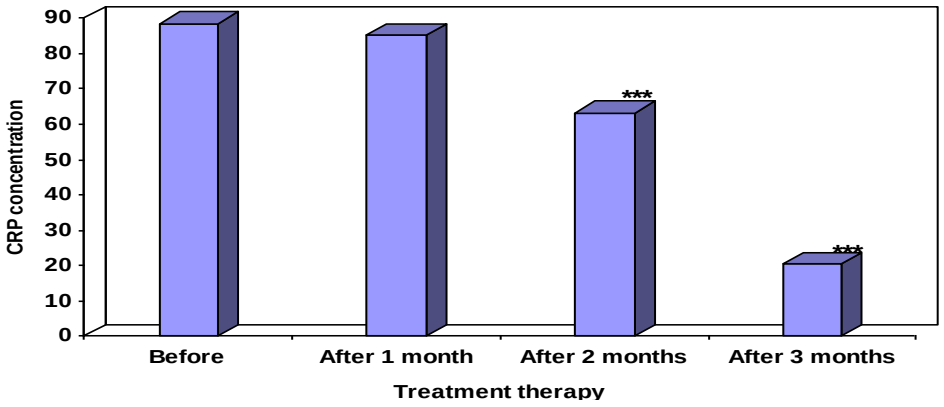


***** Significant difference from before at p<0.001**

Figure (1) CA125 concentrations in patients before therapy and a

Table 3 : Distribution of CA125 results in patients before and during therapy.

CA 125	Before therapy		After 1 month		After 2 months		After 3 months	
	No.	%	No.	%	No.	%	No.	%
+ve	44	100	44	100	17	38.6	5	11.4
-ve	0	0.0	0	0.0	27	61.4	39	88.6



***** Significant difference from before at p<0.001**

Figure (2) CRP concentrations in patients before therapy and according to period of

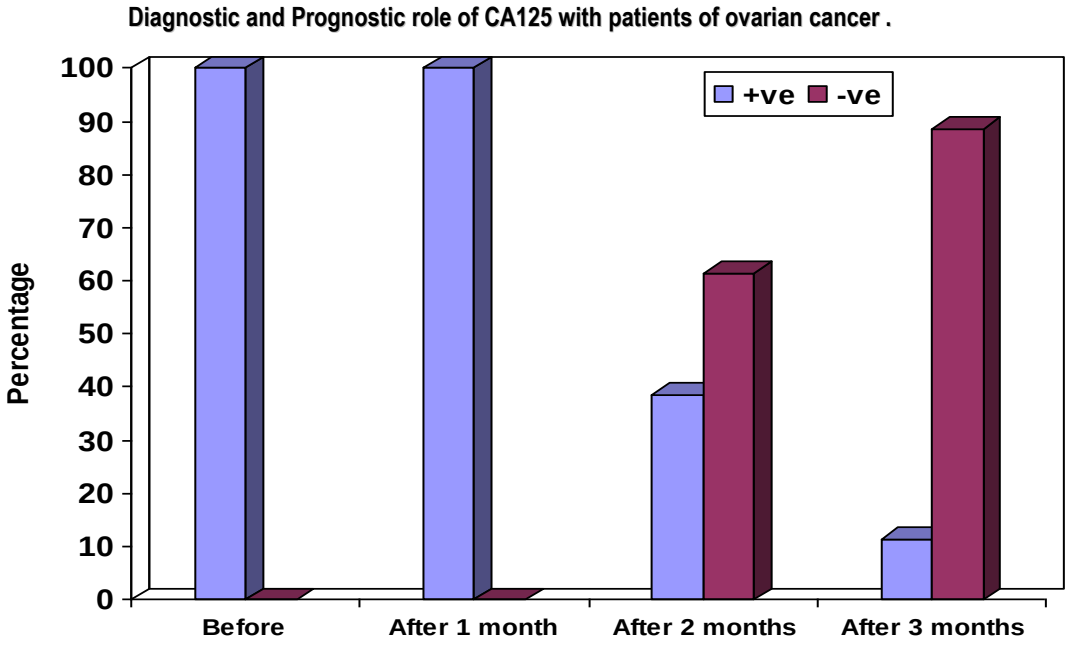


Figure (3) Distribution of CA125 results in patients before and during therapy.

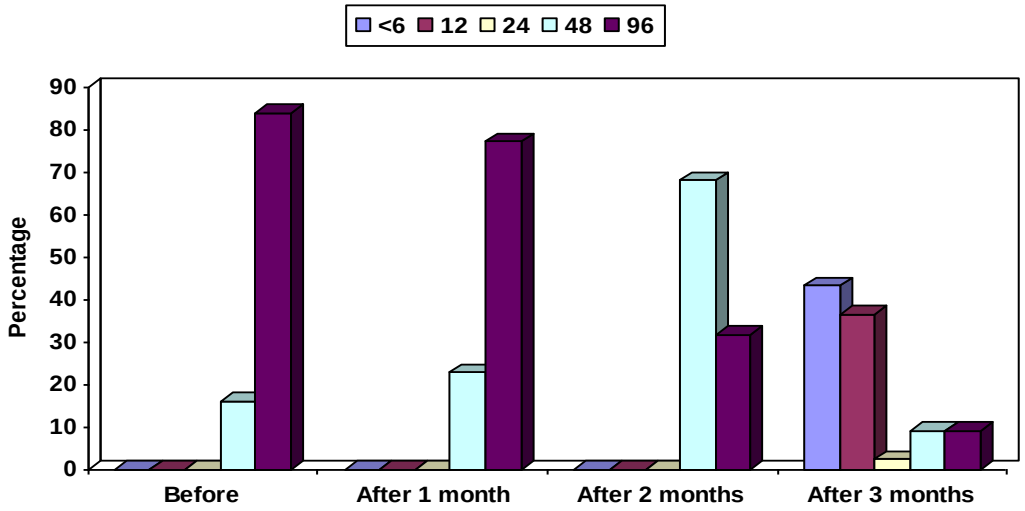


Figure (4) Distribution of CRP concentration in patients before and during therapy.

Table 4 : Relationship between CA125 and CRP results in patients.

CRP	CA125 (Mean ± SD)	Duncan group
6	17.53 ± 5.50	A
12	16.93 ± 5.10	A
48	38.09 ± 21.45	B
96	58.08 ± 22.58	C

Different letters mean significant difference at $p \leq 0.05$ according to Duncan test

Table 5 : Sensitivity and specificity of CA125 and CRP as a diagnostic indicators of the disease.

		CA125				CRP			
		≥30		<30		≥6		<6	
		NO.	%	NO.	%	NO.	%	NO.	%
Disease	+	44	100	0	0.0	44	100	0	0.0
	-	20	44.4	25	55.6	30	66.7	15	33.3
Sensitivity		100.0%				100.0%			
specificity		55.6%				33.3%			
P-value		<0.001				<0.001			